Pergamon

*Phytochemistry*, Vol. 49, No. 5, pp. 1449–1451, 1998

Printed in Great Britain
0031–9422/98/\$—see front matter

**PII: S0031–9422(98)00083–1**

# TROPANE ALKALOIDS WITH A UNIQUE TYPE OF ACYL MOIETY FROM TWO *CONVOLVULUS* SPECIES¶

KRISTINA JENETT-SIEMS, PETRA MANN, MACKI KALOGA, KARSTEN SIEMS,† JASMIN JAKUPOVIC,‡
LUDGER WITTE§ and ECKART EICH*

Institut für Pharmazie II (Pharmazeutische Biologie), Freie Universität Berlin, Königin-Luise-Str. 2+4, D-14195 Berlin, Germany; † AnalytiCon AG, NL Potsdam, Hermannswerder Haus 17, D-14473 Potsdam, Germany; ‡ Institut für Organische Chemie, Technische Universität Berlin, Str. d. 17. Juni, D-10623 Berlin, Germany; § Institut für Pharmazeutische Biologie, Technische Universität Braunschweig, Mendelssohnstr. 1, D-38106 Braunschweig, Germany

(*Received in revised form* 5 *January* 1998)

**Key Word Index**—*Convolvulus siculus*; *C. sabatius* ssp. *mauritanicus*; Convolvulaceae; tropane alkaloids; tropan-3α-ol ( = tropine) esters; consiculine; consabatine; merresectine B; consiculic acid; isolation.

**Abstract**—An investigation of the roots of *Convolvulus siculus* and *C. sabatius* ssp. *mauritanicus* afforded two new tropan-3α-ol esters named consiculine and consabatine and the known base merresectine B (**3**). The acyl residues of the new alkaloids are formed by consiculic acid ( = 1β,2α-dihydroxy-5-prenyl-cyclohex-5-en-4-one carboxylic acid) and its 2-deoxy derivative, respectively. © 1998 Elsevier Science Ltd. All rights reserved

## INTRODUCTION

The first occurrence of tropane alkaloids in the genus *Convolvulus* was reported in the thirties when Orechoff and Konowalowa isolated convolvine and convolamine from the seeds of *C. pseudocantabricus* Schrenk, a widespread weed of Middle Asia [2, 3]. These compounds were characterised as *nor*tropan-3α-yl veratrate and its *N*-methyl derivative [3, 4]. Later, the same alkaloids were reisolated from *C. lineatus* L. and, together with closely related alkaloids having a veratroyl or a vanilloyl moiety as the acyl component, from *C. krauseanus* Regel et Schmalh. and *C. subhirsutus* Regel et Schmalh., also of Middle Asian origin [5–8]. Recently the first tropan-3β-ol ( = pseudotropine) ester within the Convolvulaceae was characterised: the β-isomer of phyllalbine from *C. cneorum* L. [9]. Interestingly, *C. arvensis* L., perhaps the best-known bindweed of the temperate zones, is only able to synthesise simple tropane alkaloids like tropan-3-one or tropan-3β-ol [10, 11]. Additionally, simple hydrophilic *nor*tropanes, the glycosidase inhibiting calystegines, were reported from the genus *Convolvulus* [12, 13].

In the present study we report the isolation and structural elucidation of two novel tropane alkaloids as well as the known merresectine B from *C. siculus* L., a smaller herbaceous twiner, and *C. sabatius* Viv. ssp. *mauritanicus* (Boiss.) Murb., a suffrutex used as an ornamental. Both are of Mediterranean origin (Sicily, Northwest Africa).

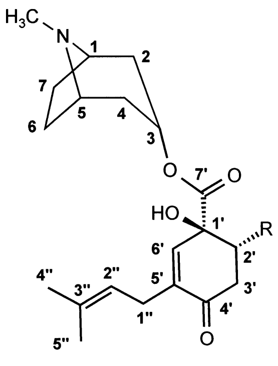
## RESULTS AND DISCUSSION

The roots of *C. siculus* contain substances **1** and **3**, those of *C. sabatius* ssp. *mauritanicus* **2** and **3**, respectively. Compound **3** turned out to be the known alkaloid merresectine B, which had first been discovered as a constituent of the tropical bindweed *Merremia dissecta* (Jacq.) Hallier f. [14], by comparison with an authentic sample. Structure elucidation of compounds **1** and **2** was achieved using extensive MS and NMR methods. The HRMS spectrum of compound **1** showed a molecular weight of 363.20413 (calc. 363.20457) from which a molecular formula of $C_{20}H_{29}NO_5$ could be established, whereas the weight of **2** was 16 mass units lower. The base peak at *m*/*z* 124 and characteristic fragments at *m*/*z* 140, 96, and 83 in the EIMS spectrum suggested that **1** and **2** could be tropan-3-ol esters. This was confirmed by the $^1$H and $^{13}$C NMR data. The β configuration of H-3 was indicated by the triplet at δ 5.11. In the $^1$H NMR spectrum the acyl moiety of **1** was characterised by two short sequences: (i) one starting with an olefinic proton at δ 6.30 which coupled allylically to the methylene protons of a prenyl group and (ii) a proton

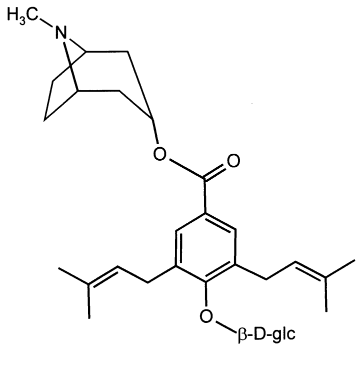
---

¶ Part 5 in the series "Phytochemistry and Chemotaxonomy of the Convolvulaceae". For part 4, see ref. [1]. Presented in part at the 45th Annual Congress of the Society for Medicinal Plant Research, 1997, Regensburg, Germany.

* Author to whom correspondence should be addressed.



**1** R = OH
**2** R = H



**3**

geminal to a hydroxyl group coupled with a further methylene group. The $^{13}C$ NMR spectrum displayed three additional signals for a α,β-unsaturated ketone, a carboxylic group and a tertiary alcohol. These components could be connected to a cyclohexenone derivative. The position of the secondary hydroxyl group at C-2′ was deduced from the long range correlation between H-2′ and C-7′. The couplings of H-2′ indicated its axial orientation, whereas a NOE between the tertiary hydroxyl and H-2′ is only possible with an equatorially oriented hydroxyl group. We have named **1** consiculine.

The molecular formula of **2**, $C_{20}H_{29}NO_4$, was again determined by HRMS. The $^1H$ NMR spectrum of **2** shared many characteristics with that of **1**. The most striking difference was the presence of a further methylene group instead of the secondary alcohol, indicating the 2′-deoxy derivative of **1**. The $^{13}C$ NMR was in accordance with this suggestion. Thus we conclude that **2** is 2′-deoxyconsiculine (consabatine).

Alkaloids **1** and **2** represent a totally new type of tropan-3-ol esters because of their unique acyl moieties. We propose to assign to these residues the trivial names consiculic acid and 2-deoxyconsiculic acid. Nevertheless, their structural similarity to merresectine B is very conspicuous. Obviously, their acyl moieties share the same biosynthetic pathway. Whether consiculic acid might even be a precursor of nervogenic acid, the aromatic acyl residue of **3**, remains to be established. GC-MS analysis showed that the roots of *C. siculus* and the roots and epigeal parts of *C. sabatius* ssp. *mauritanicus* besides **1** and **2** contain further closely related alkaloids along with simple tropane derivatives. Interestingly, we were not able to detect any tropan-3-ol esters in four endemic *Convolvulus* species from the Canary Islands (*C. canariensis* L., *C. floridus* L. Fil., *C. glandulosus* (Webb) Hallier, *C. lopez-socasi* Svent.) nor in the Mediterranean species *C. althaeoides* L. ssp. *althaeoides*, *C. cantabrica* L. and *C. tricolor* L. ssp. *tricolor* [15]. All these species produce only simple pyrrolidine and tropane alkaloids. The ability to synthesise more complex tropane alkaloids is thus restricted to certain species within the genus *Convolvulus*.

## EXPERIMENTAL

### *General*

$^1H$ NMR (400 MHz) and $^{13}C$ NMR (100 MHz) spectra were recorded on a Bruker AC 400. EIMS direct inlet 70 eV. FAB-MS: Xe gas and DMSO/glycerol as matrix. HR-MS was measured with a Finnigan MAT 711, 80 eV.

### *Plant material*

Plants of *C. siculus* were grown in the Botanischer Garten, Freie Universität Berlin, from seeds collected on Tenerife and La Palma (Canary Islands, Spain). Plants of *C. sabatius* ssp. *mauritanicus* were bought in a nursery (PLUTA, Berlin-Marienfelde) and afterwards grown in the Botanischer Garten. Voucher specimens of both species have been deposited at the Institut für Pharmazie II (Pharmazeutische Biologie), Freie Universität Berlin.

### *Extraction and isolation*

180 g Ground roots of *C. siculus* (94 g of *C. sabatius* ssp. *mauritanicus*) were extracted three times with MeOH (80%). The alcoholic extract was concentrated under red. pres. and dissolved in aq. tartaric acid (2%). The acidic soln was extracted with $CHCl_3$ and EtOAc, its pH adjusted to 8 ($NaHCO_3$) and again extracted with $CHCl_3$. After evaporation the crude alkaloids were sepd by prep. HPLC [RP-18, MeOH–$H_2O$ (+0.5% $H_3PO_4$) mixtures] to give 5 mg of **1** and 3 mg of **3** (*C. siculus*) and 6 mg of **2** and 2 mg of **3** (*C. sabatius* ssp. *mauritanicus*), respectively.

*Consiculine* (**1**). UV $\lambda_{max}$ ($H_2O$/MeOH 6:4) nm: 250, EIMS *m/z* (rel. int. %): 363 $[M]^+$ (18), 346 (1), 265 (1), 195 (1), 140 (2), 124 (100), 96 (10), 83 (10), 82 (8); (+) FAB-MS *m/z*: 364; (−) FAB-MS *m/z*: 362; HR-

Table 1. $^{13}C$ NMR data of **1** and **2** ($CDCl_3$) and HMBC correlations of **1**

| | $^{13}C$ NMR data ($\delta$) | | HMBC correlations of |
|---|---|---|---|
| carbon | **1** | **2** | **1** |
| C-1 | 59.4 | 59.8 | *N*—$CH_3$, H-3 |
| C-2 | 36.4 | 35.2 | — |
| C-3 | 72.1 | 69.6 | — |
| C-4 | 36.6 | 35.3 | — |
| C-5 | 59.4 | 59.8 | *N*—$CH_3$, H-3 |
| C-6 | 25.4 | 25.1 | — |
| C-7 | 25.6 | 25.1 | — |
| —*N*—$CH_3$ | 40.3 | 39.1 | — |
| C-1′ | 77.9 | 72.0 | H-2′, H-3′ |
| C-2′ | 73.4 | 34.0 | H-3′, H-6′ |
| C-3′ | 42.2 | 34.1 | — |
| C-4′ | 196.6 | 197.6 | H-3′, H-1″, H-6′ |
| C-5′ | 141.1 | 140.9 | H-1″ |
| C-6′ | 141.8 | 140.9 | — |
| C-7′ | 171.0 | 173.7 | H-3, H-2′ |
| C-1″ | 27.2 | 27.4 | H-6′, H-2″ |
| C-2″ | 119.4 | 119.6 | H-1″, H-4″, H-5″ |
| C-3″ | 135.0 | 134.8 | H-1″, H-4″, H-5″ |
| C-4″ | 25.8 | 25.8 | H-2″ |
| C-5″ | 17.7 | 17.7 | H-2″, H-4″ |

MS *m*/*z*: 363.20413 $[M]^{+\cdot}$ ($C_{20}H_{29}NO_5^{+\cdot}$, calc. 363.20457), 195.10206 ($C_{11}H_{15}O_3^{+}$, calc. 195.10212), 124.11260 ($C_8H_{14}N^{+}$, calc. 124.11262); $^1H$ NMR ($CDCl_3$): $\delta$ (ppm) 1.55 (2 H, *m*, H-6a, H-7a), 1.61 (3 H, *br s*, H-5″), 1.74 (3 H, *br s*, H-4″), 1.74 (2 H, *m*, H-2a, H-4a), 1.97 (2 H, *m*, H-6b, H-7b), 2.22 (2 H, *m*, H-2b, H-4b), 2.26 (3H, *s*, —*N*—$CH_3$), 2.92 (2 H, *m*, 2 × H-3′), 2.94 (2 H, *br d*, $J = 7.0$ Hz, 2 × H-1″), 3.08 (1 H, *br s*, H-1/H-5), 3.11 (1 H, *br s*, H-1/H-5), 4.25 (1 H, *dd*, $J = 8.0$ Hz, 11.0 Hz, H-2′), 5.10 (1 H, *br t*, $J = 7.0$ Hz, H-2″), 5.11 (1 H, *t*, $J = 5.0$ Hz, H-3), 6.30 (1 H, *br t*, $J = 1.5$ Hz, H-6′); $^{13}C$ NMR (Table 1).

*Consabatine* (**2**). UV $\lambda_{max}$ ($H_2O$/MeOH 1:1) nm: 255; EIMS *m*/*z* (rel. int. %): 347 $[M]^+$ (31), 330 (3), 223 (1), 141 (10), 140 (3), 124 (100), 96 (16), 83 (10), 82 (15); (+) FAB-MS *m*/*z*: 348 $[M+H]^+$; HR-MS *m*/*z*: 347.20949 $[M]^{+\cdot}$ ($C_{20}H_{29}NO_4^{+\cdot}$, calc. 347.20966), 330.20658 ($C_{20}H_{28}NO_3^{+\cdot}$ calc. 330.20692), 223.09710 ($C_{12}H_{15}O_4^{+}$, calc. 223.09704), 141.11535 ($C_8H_{15}NO^{+\cdot}$, calc. 141.11536), 124.11260 ($C_8H_{14}N^{+}$, calc. 124.11262); $^1H$ NMR ($CDCl_3$): $\delta$ (ppm) 1.63 (3 H, *s*, H-5″), 1.75 (3 H, *s*, H-4″), 1.79 (2 H, *br d*, $J = 15.0$ Hz, H-2a, H-4a), 1.86 (2 H, *m*, H-6a, H-7a), 2.11 (2 H, *m*, H-6b, H-7b), 2.24 (1 H, *m*, H-2′a), 2.39 (1 H, *m*, H-2′b), 2.47 (3 H, *s*, —*N*—$CH_3$), 2.52 (2 H, *m*, H-2b, H-4b), 2.64 (1 H, *m*, H-3′a), 2.75 (1 H, *m*, H-3′b), 2.96 (2 H, *br d*, $J = 7.0$ Hz, 2 × H-1″), 3.42 (2 H, *br s*, H-1, H-5), 5.11 (1 H, *t*, $J = 7.0$ Hz, H-2″), 5.16 (1 H, *t*, $J = 5.0$ Hz, H-3), 6.42 (1H, *br s*, H-6′); $^{13}C$ NMR (Table 1).

*Merresectine B* (**3**). This was identified by comparison of its chromatographic and spectral properties with an authentic sample.

*Acknowledgements*—The authors are indebted to Prof. Dr W. Greuter, Botanischer Garten, Freie Universität Berlin, for identification of *C. sabatius* ssp. *mauritanicus*, to Mrs E. Bäumel-Eich for essential support in exploring and collecting the plant material on the Canary Islands, and to Mrs U. Ostwald, Institut für Organische Chemie, Freie Universität Berlin, for measurements of HR-MS and FAB mass spectra.

## REFERENCES

1. Jenett-Siems, K., Schimming, T., Kaloga, M., Eich, E., Siems, K., Gupta, M. P., Witte, L. and Hartmann, T., *Phytochemistry*, 1998, **47**, 1551.
2. Orechoff, A. and Konowalowa, R., *Archiv der Pharmazie* (*Weinheim*), 1933, **271**, 145.
3. Orechoff, A. and Konowalowa, R., *Berichte der Deutschen Chemischen Gesellschaft* (*Chemische Berichte*), 1934, **67**, 1153.
4. Orechoff, A. and Konowalowa, R., *Berichte der Deutschen Chemischen Gesellschaft* (*Chemische Berichte*), 1935, **68**, 814.
5. Israilov, I., Abduazimov, K. A. and Yunosov, S. Y., *Doklady Akademii Nauk UzSSR* (*Doklady Akademii Nauk Republiki Uzbekistan*), 1965, **22**, 18.
6. Aripova, S. F., Malikov, V. M. and Yunosov, S. Y., *Khimiya Prirodnykh Soedinenii*, 1977, 290.
7. Aripova, S. F., Sharova, E. G., Yunosov, S. Y. and Dzabbarov, A., *Khimiya Prirodnykh Soedinenii*, 1983, 245.
8. Aripova, S. F. and Yunusov, S. Y., *Khimiya Prirodnykh Soedinenii*, 1986, 618.
9. Mann, P., Kaloga, M. and Eich, E., *43rd Congress on Medicinal Plant Research*, Halle, 1995, Abstract Book, p. 61.
10. Jenett-Siems, K. and Eich, E., *European Journal of Pharmaceutical Sciences*, 1994, **2**, 122.
11. Todd, F. G., Stermitz, F. R., Schultheis, P., Knight, A. P. and Traub-Dargatz, J., *Phytochemistry*, 1995, **39**, 301.
12. Goldmann, A., Milat, M. L., Ducrot, P. H., Lallemand, J. Y., Maille, M., Lepingle, A., Charpin, L. and Tepfer, D., *Phytochemistry*, 1990, **29**, 2125.
13. Schimming, T., Mann, P., Richter, A., Tofern, B., Jenett-Siems, K., Dräger, B., Asano, N., Gupta, M. P., Correa A., M.D. and Eich, E., *Phytochemistry*, submitted.
14. Weigl, R., Kaloga, M. and Eich, E., *Planta Medica*, 1992, **58**, (Suppl.) A, 705.
15. Jenett-Siems, K., Dissertation Fachbereich Pharmazie, Freie Universität Berlin, 1996.